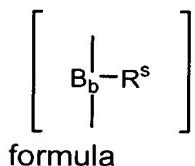


We claim:

1. A method for producing an array of immobilized nucleic acids on an active location array device comprising a plurality of activatable locations on a support material, the method comprising:
 - 5 a) activating a first set L_1 of locations on the active array device, wherein at least some of the activated locations comprise a predetermined synthetic addressing unit (SAU) or set of synthetic addressing units attached at the locations, and wherein the activation of the locations creates a condition favorable to the binding of the SAUs to SBUs;
 - 10 b) contacting the activated set of locations with a first set C_1 of synthetic binding unit (SBU)- nucleic acid (NA) conjugates, wherein at least some of the SBUs in the set of conjugates are capable of specifically binding to at least some of the SAUs attached at the activated locations;
 - c) removing the unbound conjugates; and
 - 15 d) repeating steps (a) through (c) M number of times, activating set L_{M+1} of locations, and contacting them with set C_{M+1} of conjugates, wherein $M \geq 1$.
2. The method of claim 1 wherein the same SAU is attached to at least two activatable locations, wherein the locations are each in a different set L.
3. The method of claim 2 wherein the activated locations are in rectangular array on the support material.
- 20 4. The method of claim 3 wherein, for at least a portion of the rectangular array, rows of locations have the same SAU, and columns of locations are activated as sets L.
5. The method of claim 3 wherein rectangular groups of locations are activated as sets L.
- 25 6. The method of claim 1 wherein the active location array is an active electronic array, wherein each locations of the array has associated therewith an electrode, and wherein each location is activated by the electronic biasing of the associated electrode.

7. The method of claim 6 wherein step (c) further comprises reversing the bias of the electrodes at the set of activated locations to electronically wash away unbound conjugates.
8. The method of claim 7 wherein a counter-electrode is utilized as a collection point for the unbound conjugates.
- 5 9. The method of claim 8 wherein one or more SAUs are attached to the counter electrode to collect the electronically washed conjugates.
- 10 10. The method of claim 1 wherein the SBUs of the conjugates in the sets C are oligomers comprised of monomeric units, the monomeric units having the general



10 wherein B_b is a backbone moiety which connects the monomeric unit to the oligomer, and wherein R^s is a specific recognition moiety which provides the molecular interaction which allows the SBU to specifically interact with the corresponding synthetic addressing unit.

- 15 11. The method of claim 10 wherein B_b comprises a 6 membered ring containing carbon.
12. The method of claim 10 wherein B_b comprises a six membered ring selected from the group consisting of a pyranosyl ring and a cyclohexyl ring.
- 20 13. The method of claim 10 wherein R^s provides the molecular interaction through hydrogen bonds or base stacking.
14. The method of claim 10 wherein R^s comprises a nitrogen heterocycle moiety.
15. The method of claim 10 wherein the synthetic binding units (SBUs) of the conjugates of the sets C are selected from the group consisting of p-RNAs, p-DNAs, and CNA's.
- 25

16. The method of claim 15 wherein the synthetic binding units (SBUs) of the conjugates of the sets C are pRNA or pDNA, and wherein the SBUs are linked via their 2' ends with the 5' ends of the nucleic acids (NA).
- 5 17. The method of claim 15 wherein the synthetic binding units (SBUs) of the conjugates of the sets C are pRNA or pDNA, and wherein the SBUs are linked via their 2' ends with the 3' ends of the nucleic acids (NA).
- 10 18. The method of claim 15 wherein the synthetic binding units (SBUs) of the conjugates of the sets C are pRNA or pDNA, and wherein the SBUs are linked via their 4' ends with the 3' ends of the nucleic acids (NA).
- 15 19. The method of claim 15 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 4' end with the 5' end of the nucleic acid (NA).
20. The method of claim 1 wherein the nucleic acids (NA) of the conjugates are selected from the group consisting of deoxyribonucleic acids and ribonucleic acids, and chemically modified nucleic acids.
- 15 21. The method of claim 1 wherein the nucleic acids (NA) of the conjugates are selected from the group consisting of phosphorothioate nucleic acids, phosphorodithioate nucleic acids, methylphosphonate nucleic acids, 2'-O-methyl RNA, and 2'-fluoro RNA.
- 20 22. The method of claim 1 wherein the nucleic acids (NA) of the conjugates are selected from the group consisting of peptide nucleic acids (PNA) and locked nucleic acids (LNA.)
23. The method of claim 1 wherein the nucleic acids (NA) of the conjugates are selected from the group consisting of an aptamer and an aptazyme.
- 25 24. The method of claim 1 wherein the conjugates further comprise at least one labeling moiety.
25. The method of claim 24 wherein the labeling moiety is selected from the group consisting of fluorescent moieties, quencher moieties, visible dye moieties, radioactive moieties, chemiluminescent moieties, biotin moieties, hapten moieties, micro-particles, paramagnetic micro-particles, and enzymatic labeling moieties.
- 30

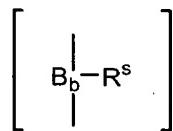
- 5 26. The method of claim 25 wherein the labeling moiety is a fluorescent dye moiety selected from the group consisting of: BODIPY™ dyes, cyanine dyes, Alexa™ dyes, fluorescein dyes, rhodamine dyes, phycoerythrin dyes, coumarin dyes, Texas Red dyes, Lissamine™, FAM, HEX, TET, TAMRA, ROX, EDANA, 4-Acetamido-4'-isothiocyanato-stilbene-2,2'-disulfonic acid, 4,4'-Diisothiocyanatostilbene-2,2'-disulfonic acid, Succinimidyl pyrene butyrate, Acridine isothiocyanate, Cascade Blue, Oregon Green, Lucifer Yellow vinyl sulfone, and IR1446 (Kodak™ Laser Dye).
- 10 27. The method of claim 25 wherein the labeling moiety is a quencher moiety selected from the group consisting of Black Hole Quencher™ moieties, DABCYL, Reactive Red 4 (Cibacron Brilliant Red 3B-A), Malachite Green, 4-Dimethylaminophenylazophenyl-4'-isothiocyanate (DABITC), and 4,4'-Diisothiocyanatodihydro-stilbene-2,2'-disulfonic acid moieties.
- 15 28. The method of claim 1 wherein the synthetic address units (SAUs) attached to the activated locations comprise an oligomer selected from the group consisting of p-RNAs, p-DNAs and CNAs.
- 20 29. The method of claim 1 wherein at least 10 distinct nucleic acids are immobilized.
30. The method of claim 1 wherein at least 100 distinct nucleic acids are immobilized.
- 25 31. The method of claim 1 wherein at least 1000 distinct nucleic acids are immobilized.
32. The method of claim 1 wherein at least 10,000 distinct nucleic acids are immobilized.
33. The method of claim 1 wherein each activated location has a single SAU attached at that location.
34. The method of claim 1 wherein at least one activated location has a known mixture of SAUs attached at that location.
35. The method of claim 1 wherein the support material comprises a material selected from the group consisting of silicon, silicon dioxide, silicon nitride, controlled porosity glass, metal, metal silicilide, inorganic sol-gels, and hydrogels.

36. The method of claim 1 wherein the support material comprises a hydrogel selected from the group consisting of agarose, polyacrylamide, polymethacrylamide, and organic polymer hydrogels.
- 5 37. The method of claim 1 wherein the support material is a permeation layer over an electrode of an active electronic array.
38. The method of claim 1 wherein the synthetic address units (SAU) are attached to the support material via a biotin/streptavidin interaction.
- 10 39. The method of claim 1 wherein the synthetic address units (SAU) are attached to the support material via at least one covalent bond.
40. The method of claim 39 wherein the covalent bond is formed by reacting a hydrazide group on the synthetic address units (SAU) with a functional group on the support.
- 15 41. The method of claim 1 wherein the SBU portions of the conjugate members of each set C are orthogonal.
42. The method of claim 1 wherein each set C comprises at least five conjugates.
43. The method of claim 1 wherein each set C comprises at least ten conjugates.
44. The method of claim 1 wherein each set C comprises at least twenty conjugates.
- 20 45. The method of claim 1 wherein each set C comprises at least 100 conjugates.
46. The method of claim 1 wherein each NA sequence in each set C is conjugated to a specific SBU.
47. The method of claim 1 wherein each SBU in each set C is conjugated to a specific NA sequence.
- 25 48. The method of claim 1 wherein each NA sequence in each set C is conjugated to a specific SBU, and each SBU is conjugated to a specific NA sequence.
49. The method of claim 1 wherein each NA sequence in each set C is conjugated to a set of SBUs.
50. The method of claim 1 wherein each SBU in each set C is conjugated to a set of NA sequences.
51. The method of claim 1 wherein M is an integer between 1 and 100.

52. The method of claim 1 wherein M is an integer between 1 and 20.
53. The method of claim 1 wherein M is an integer between 1 and 10.
54. The method of claim 1 wherein the conjugates are contacted with a sample before being contacted with the support.
- 5 55. The method of claim 54 wherein the sample is a biological sample.
56. The method of claim 55 wherein the biological sample is derived from a sample selected from the group consisting of human materials, animal materials, plant materials, fungal materials, cell cultures, viral cultures, food samples, and water samples.
- 10 57. The method of claim 55 wherein more than one set of conjugates is contacted with more than one biological sample, wherein nucleic acids of each biological sample which hybridize to nucleic acids of the conjugates are sorted by the SBUs of the conjugates to known locations on the support material.
- 15 58. The method of claim 57 wherein in each set C of conjugates, prior to contact with the biological sample, the same nucleic acid sequence of the conjugates is conjugated to the same SBU.
59. The method of claim 57 wherein each biological sample is obtained under differing conditions for the biological material sampled, and wherein the sorting of the hybridized nucleic acids from each sample by the pairing of the SBUs to the SAUs produces a gene expression pattern.
- 20 60. The method of claim 54 wherein the conjugates are utilized as primers in an enzymatic amplification reaction while contacted with the biological sample.
61. The method of claim 1 further comprising, after completing steps (a) through (c) at least once, incubating the support with a sample containing target nucleic acids and with reagents for detecting binding of targets to the conjugates.
- 25 62. The method of claim 61 wherein the sample is a biological sample.
63. The method of claim 62 wherein the biological sample is derived from a sample selected from the group consisting of human materials, animal materials, plant materials, fungal materials, cell cultures, viral cultures, food samples, and water samples.

64. The method of claim 61 further comprising the step of detecting the target nucleic acids hybridized to the nucleic acids of conjugates immobilized on the support material.
- 5 65. The method of claim 64 further comprising the step of removing, after detecting the hybridized nucleic acids, the conjugates and sample from the support material by destabilizing the association between the SBUs and the SAUs.
- 10 66. A supermolecular construct comprising:
 - at least one synthetic address unit (SAU) attached to a support material comprising an array of discreet locations, wherein the same SAU is attached to at least two predetermined locations on the support material, and
 - at least two conjugates comprising a synthetic binding unit (SBU) and a nucleic acid (NA), wherein at least two of the conjugates have the same SBU and different NAs,
 - wherein the SBU of the conjugates form a synthetic binding system unit (SBS) with the SAU at the two predetermined locations, and immobilize each of the two different NAs at a different location.
- 15 67. The supermolecular construct of claim 66 wherein the SBU and the SAU each comprise an at least partially complementary sequence of monomeric units which non-covalently associate with one another in a sequence-dependent manner.
- 20 68. The supermolecular construct of claim 66 wherein the synthetic address unit (SAU) comprises, independently of the synthetic binding unit (SBU), an oligomer selected from the group consisting of p-RNAs, p-DNAs and CNAs.
- 25 69. The supermolecular construct of claim 66 comprising at least five different conjugates immobilized by the same SBS.
70. The supermolecular construct of claim 66 comprising at least ten different conjugates immobilized by the same SBS.
71. The supermolecular construct of claim 66 comprising at least 100 different conjugates immobilized by the same SBS.

72. The supermolecular construct of claim 66 comprising at least 10 different immobilized nucleic acids.
73. The supermolecular construct of claim 66 comprising at least 100 different immobilized nucleic acids.
- 5 74. The supermolecular construct of claim 66 comprising at least 1000 different immobilized nucleic acids.
75. The supermolecular construct of claim 66 comprising at least 10,000 different immobilized nucleic acids.
- 10 76. The supermolecular construct of claim 66 wherein at least one discreet location has a known mixture of SAUs attached at that location.
77. The supermolecular construct of claim 66 wherein the support material comprises a material selected from the group consisting of silicon, silicon dioxide, silicon nitride, controlled porosity glass, metal, metal silicilide, inorganic sol-gels, and hydrogels.
- 15 78. The supermolecular construct of claim 66 wherein the support material comprises a hydrogel selected from the group consisting of agarose, polyacrylamide, polymethacrylamide, and organic polymer hydrogels.
79. The supermolecular construct of claim 66 wherein the support material is a permeation layer over an electrode of an active electronic array.
- 20 80. The supermolecular construct of claim 66 wherein the synthetic address units (SAU) are attached to the support material via a biotin/streptavidin interaction.
81. The supermolecular construct of claim 66 wherein the synthetic address units (SAU) are attached to the support material via at least one covalent bond.
- 25 82. The supermolecular construct of claim 81 wherein the covalent bond is formed by reacting a hydrazide group on the synthetic address units (SAU) with a functional group on the support.
83. The supermolecular construct of claim 66 wherein the SBUs of the conjugates are oligomers comprised of monomeric units, the monomeric units having the



general formula

wherein B_b is a backbone moiety which connects the monomeric unit to the oligomer, and wherein R^s is a specific recognition moiety which provides the molecular interaction which allows the SBUs to specifically interact with their corresponding synthetic addressing unit.

- 5 84. The supermolecular construct of claim 83 wherein B_b comprises a 6 membered ring containing carbon.
- 10 85. The supermolecular construct of claim 83 comprises a six membered ring selected from the group consisting of a pyranosyl ring and a cyclohexyl ring.
- 15 86. The supermolecular construct of claim 83 wherein R^s provides the molecular interaction through hydrogen bonds or base stacking.
- 20 87. The supermolecular construct of claim 83 wherein R^s comprises a nitrogen heterocycle moiety.
- 25 88. The supermolecular construct of claim 83 wherein at least one synthetic binding unit (SBU) is selected from the group consisting of p-RNAs, p-DNAs, and CNA's.
90. 89. The supermolecular construct of claim 88 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 2' end with the 5' end of the nucleic acid (NA).
91. 90. The supermolecular construct of claim 88 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 2' end with the 3' end of the nucleic acid (NA).
92. 91. The supermolecular construct of claim 88 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 4' end with the 3' end of the nucleic acid (NA).
93. 92. The supermolecular construct of claim 88 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 4' end with the 5' end of the nucleic acid (NA).

93. The supermolecular construct of claim 66 wherein the nucleic acids (NA) of the conjugates are selected from the group consisting of deoxyribonucleic acids, ribonucleic acids, and chemically modified nucleic acids.
- 5 94. The supermolecular construct of claim 66 wherein the nucleic acids (NA) of the conjugates are selected from the group consisting of phosphorothioate nucleic acids, phosphorodithioate nucleic acids, methylphosphonate nucleic acids, 2'-O-methyl RNA, and 2'-fluoro RNA.
- 10 95. The supermolecular construct of claim 66 wherein the nucleic acids (NA) of the conjugates are selected from the group consisting of peptide nucleic acids (PNA) and locked nucleic acids (LNA.)
- 15 96. The supermolecular construct of claim 66 wherein the nucleic acids (NA) of the conjugates are selected from the group consisting of an aptamer and an aptazyme.
- 20 97. The supermolecular construct of claim 66 wherein the conjugates further comprising at least one labeling moiety.
98. The supermolecular construct of claim 97 wherein the labeling moiety is selected from the group consisting of fluorescent moieties, quencher moieties, visible dye moieties, radioactive moieties, chemiluminescent moieties, biotin moieties, hapten moieties, micro-particles, paramagnetic micro-particles, and enzymatic labeling moieties.
- 25 99. The supermolecular construct of claim 98 wherein the labeling moiety is a fluorescent dye moiety selected from the group consisting of: BODIPY™ dyes, cyanine dyes, Alexa™ dyes, fluorescein dyes, rhodamine dyes, phycoerythrin dyes, coumarin dyes, Texas Red dyes, Lissamine™, FAM, HEX, TET, TAMRA, ROX, EDANA, 4-Acetamido-4'-isothiocyanato-stilbene-2,2'-disulfonic acid, 4,4'-Diisothiocyanatostilbene-2,2'-disulfonic acid, Succinimidyl pyrene butyrate, Acridine isothiocyanate, Cascade Blue, Oregon Green, Lucifer Yellow vinyl sulfone, and IR1446 (Kodak™ Laser Dye).
- 30 100. The supermolecular construct of claim 98 wherein the labeling moiety is a quencher moiety selected from the group consisting of Black Hole Quencher™ moieties, DABCYL, Reactive Red 4 (Cibacron Brilliant Red 3B-A), Malachite

Green, 4-Dimethylaminophenylazophenyl-4'-isothiocyanate (DABITC), and 4,4'-Diisothiocyanatodihydro-stilbene-2,2'-disulfonic acid moieties.

101. The supermolecular construct of claim 66 wherein at least two different SAUs are attached to at least three different locations, and wherein the non-identical SAUs
5 are orthogonal.

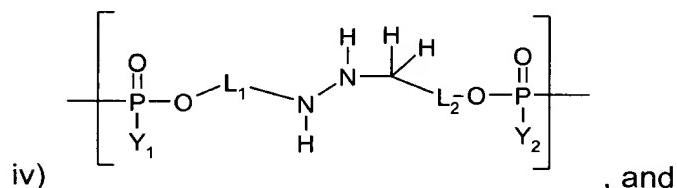
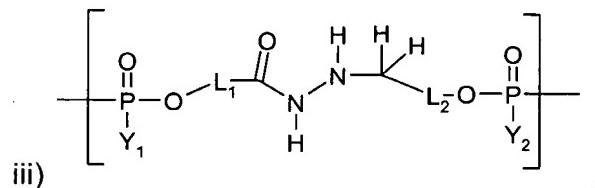
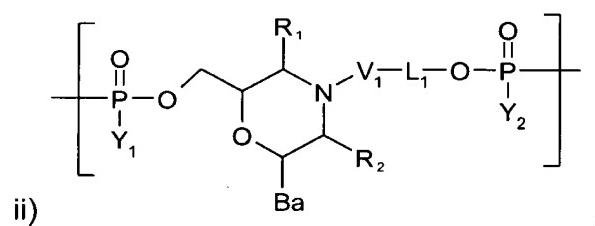
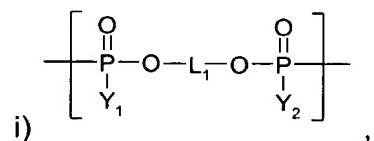
102. A conjugate with the general formula (NA)(SBU) wherein:

NA is a nucleic acid,

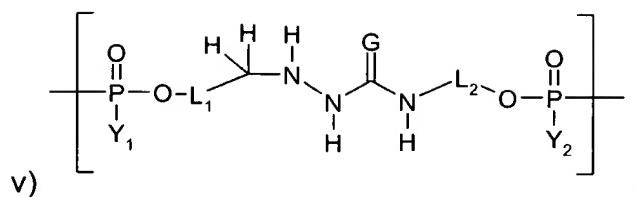
SBU is a synthetic binding unit,

wherein each NA is linked to at least one SBU by a linker X, wherein X

10 is selected from the group consisting of:



RECEIVED
U.S. PATENT AND TRADEMARK OFFICE
MAY 2013



wherein

- Y₁, Y₂ are independently of one another OH; SH, NH₂ or CH₃,
- G is O or S,
- L₁, L₂ are independently linkers selected from the group consisting of:
a covalent bond; and a linker chain moiety comprising a saturated or unsaturated, branched or unbranched, substituted or unsubstituted, chain of 1-60 carbon atoms and 0-40 heteroatoms selected from the group consisting of N, O, and S;
- V₁, V₂ are independently selected from the group consisting of
-[-CH₂-]-, and
-
- R₁, R₂ are independently of one another H or OH, and wherein
- Ba is a nitrogen heterocycle moiety.

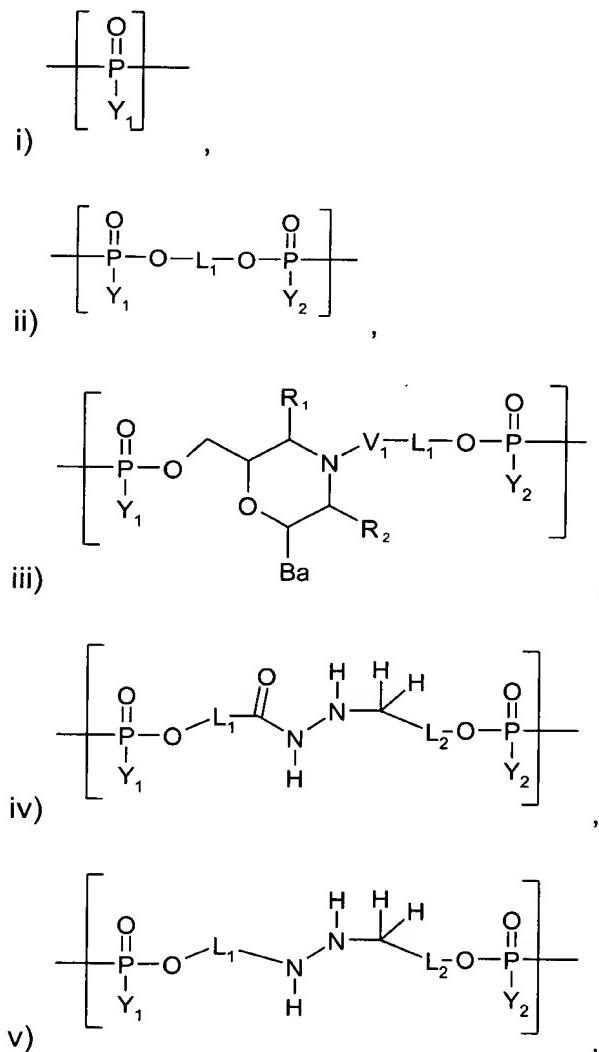
103. The conjugate of claim 102 wherein X has the general formula (i).
104. The conjugate of claim 102 wherein X has the general formula (ii).
105. The conjugate of claim 102 wherein X has the general formula (iii).
- 5 106. The conjugate of claim 102 wherein X has the general formula (iv).
107. The conjugate of claim 102 wherein X has the general formula (v).
108. A conjugate with the general formula (NA)_n(SBU)_m, wherein:

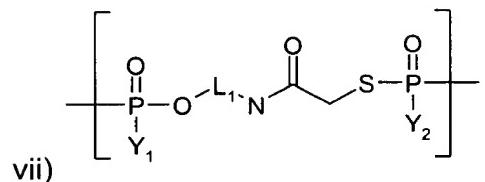
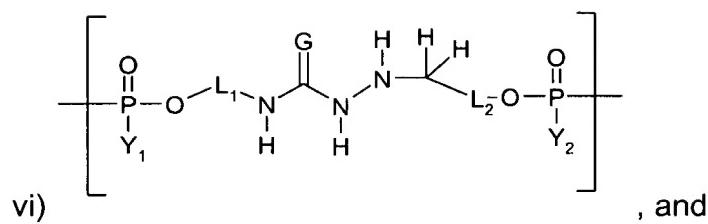
NA is a nucleic acid,

SBU is a synthetic binding unit,

wherein each NA is linked to at least one SBU, n is an integer from 1 to 6, m is an integer from 1 to 6, and wherein n + m > 2.

109. The conjugate of claim 108 wherein for $(NA)_n(SBU)_m$, $n \geq 2$.
110. The conjugate of claim 108 wherein for $(NA)_n(SBU)_m$, $m \geq 2$.
- 5 111. The conjugate of claim 108 wherein for $(NA)_n(SBU)_m$, $m + n \geq 4$.
112. The conjugate of claim 108, wherein each NA is covalently linked to at least one SBU via a linker moiety X or a branching moiety W, wherein
X, independently for each linker unit, is selected from the group consisting of:





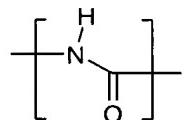
wherein

Y_1, Y_2 are independently of one another OH, SH, NH₂ or CH₃,

G is O or S,

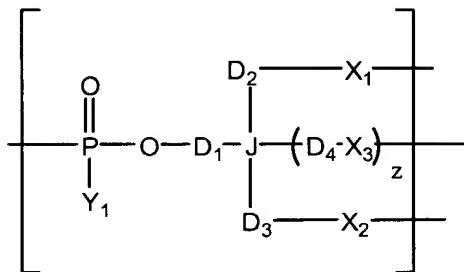
L_1, L_2 are independently linkers selected from the group consisting of:
a covalent bond; and a linker chain moiety comprising a saturated or unsaturated, branched or unbranched, substituted or unsubstituted, chain of 1-60 carbon atoms and 0-40 heteroatoms selected from the group consisting of N, O, and S;

V_1, V_2 are independently selected from the group consisting of
-[-CH₂-], and



R_1, R_2 are independently of one another H or OH, and
Ba is a nitrogen heterocycle moiety;

and wherein W has the general formula:



wherein Y₁ is OH, SH, NH₂ or CH₃;

wherein D₁, D₂, D₃, and D₄, are, independently, a covalent bond or a linker chain moiety comprising a saturated or unsaturated, branched or unbranched, substituted or unsubstituted, chain of 1 to 10 carbon atoms and 0 to 4 heteroatoms selected from the group consisting of O, S, and N;

wherein J is carbon or nitrogen;

wherein z is 0 or 1, further wherein z is 0 if J is nitrogen; and

wherein X_1 , X_2 , and X_3 , are independently X as described above.

113. The conjugate of claim 112 wherein $(NA)_n(SBU)_m$ has a general formula selected from the group consisting of (I), (II), or (III):

(NA)-X₁-(SBU)-X₂-(NA) (formula (I))

(SBU)-X₁-(NA)-X₂-(SBU) (formula (II)),

(NA)-W-(-(SBU))_u (formula (III)),

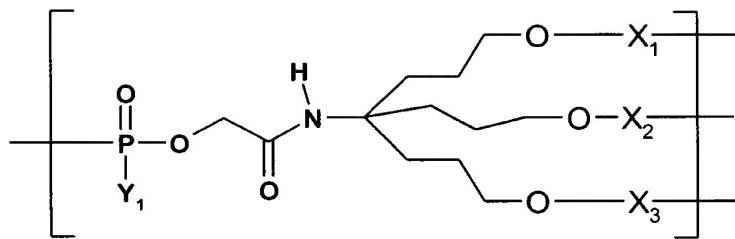
where u is an integer between 2 and 6.

114. The conjugate of claim 113 wherein $(NA)_n(SBU)_m$ has the general formula (I).

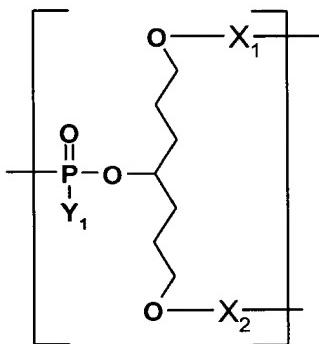
115. The conjugate of claim 113 wherein $(NA)_n(SBU)_m$ has the general formula (II).

10 116. The conjugate of claim 113 wherein $(NA)_n(SBU)_m$ has the general formula (III).

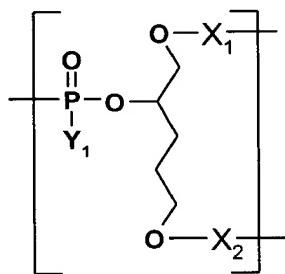
117. The conjugate of claim 112 wherein W has the general formula



118. The conjugate of claim 112 wherein W has the general formula

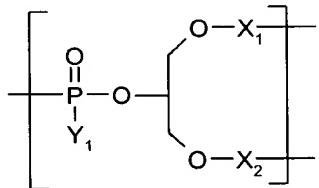


119. The conjugate of claim 112 wherein W has the general formula

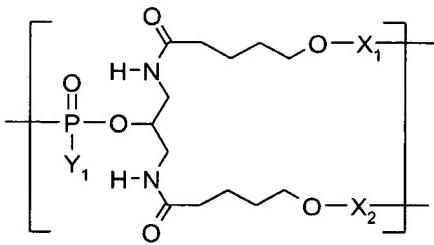


5

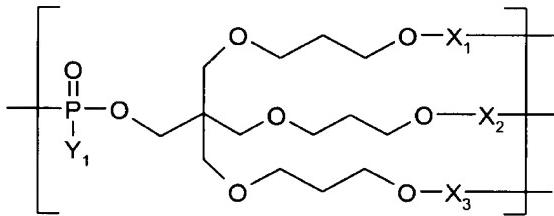
120. The conjugate of claim 112 wherein W has the general formula



121. The conjugate of claim 112 wherein W has the general formula

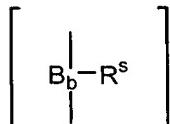


122. The conjugate of claim 112 wherein W has the general formula



123. The conjugate of claim 112 wherein at least one X has the general formula (i).
124. The conjugate of claim 112 wherein at least one X has the general formula (ii).
125. The conjugate of claim 112 wherein at least one X has the general formula (iii).
126. The conjugate of claim 112 wherein at least one X has the general formula (iv).
127. The conjugate of claim 112 wherein at least one X has the general formula (v).
128. The conjugate of claim 112 wherein at least one X has the general formula (vi).
129. The conjugate of claim 112 wherein at least one X has the general formula (vii).
130. The conjugate of claim 102 wherein each L is independently selected from the group consisting of:
a covalent bond,
-[-(CH₂)_n-],
-[-CH₂-CH₂-(O-CH₂-CH₂)_m]- ,
-[-CH₂-CH₂-CH₂-(O-CH₂-CH₂-CH₂)_q]- ,
-[-(CH₂)_v-C(O)NH-(CH₂)_z]-, and
-[-(CH₂)_v-NHC(O)-(CH₂)_z]-,
wherein n, m, q, v, z are integers between 1 and 20.
131. The conjugate of claim 130 wherein at least one L is a covalent bond.

132. The conjugate of claim 130 wherein at least one L is $-[-(CH_2)_n]-$, and wherein n is an integer between 2 and 12.
133. The conjugate of claim 130 wherein at least one L is $-[-CH_2-CH_2-(O-CH_2-CH_2)_m]-$, and wherein m is an integer between 1 and 5.
- 5 134. The conjugate of claim 130 wherein at least one L is $-[-CH_2-CH_2-CH_2-(O-CH_2CH_2-CH_2)_q]-$, and wherein q is an integer between 1 and 4.
135. The conjugate of claim 130 wherein at least one L is $-[-(CH_2)_v-C(O)NH-(CH_2)_z]-$, and wherein v and z are independently integers between 2 and 6.
- 10 136. The conjugate of claim 130 wherein at least one L is $-[-(CH_2)_v-NHC(O)-(CH_2)_z]-$, and wherein v and z are independently integers between 2 and 6.
137. The conjugate of claim 102 wherein the SBUs are oligomers comprised of



monomeric units, the monomeric units having the general formula

15 wherein B_b is a backbone moiety which connects the monomeric unit to the oligomer, and wherein R^s is a specific recognition moiety which provides the molecular interaction which allows the SBU to specifically interact with a synthetic addressing unit.

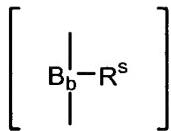
- 20 138. The conjugate of claim 137 wherein B_b comprises a 6 membered ring containing carbon.
139. The conjugate of claim 137 wherein B_b comprises a six membered ring selected from the group consisting of a pyranosyl ring and a cyclohexyl ring.
140. The conjugate of claim 137 wherein R^s provides the molecular interaction through hydrogen bonds or base stacking.
- 25 141. The conjugate of claim 137 wherein R^s comprises a nitrogen heterocycle moiety.

142. The conjugate of claim 137, wherein at least one synthetic binding unit (SBU) is selected from the group consisting of p-RNAs, p-DNAs, and CNA's.
 143. The conjugate of claim 142 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 2' end with the 5' end of the nucleic acid (NA).
 144. The conjugate of claim 142 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 2' end with the 3' end of the nucleic acid (NA).
 145. The conjugate of claim 142 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 4' end with the 3' end of the nucleic acid (NA).
 146. The conjugate of claim 142 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 4' end with the 5' end of the nucleic acid (NA).
 147. The conjugate of claim 102 wherein the nucleic acid (NA) is selected from the group consisting of deoxyribonucleic acids, ribonucleic acids, and chemically modified nucleic acids.
 148. The conjugate of claim 102 wherein the nucleic acid (NA) is selected from the group consisting of phosphorothioate nucleic acids, phosphorodithioate nucleic acids, methylphosphonate nucleic acids, 2'-O-methyl RNA, and 2'-fluoro RNA.
 149. The conjugate of claim 102 wherein the nucleic acid (NA) is selected from the group consisting of peptide nucleic acids (PNA) and locked nucleic acids (LNA.)
 150. The conjugate of claim 102 wherein the nucleic acid (NA) is selected from the group consisting of an aptamer and an aptazyme.
 151. The conjugate of claim 102, further comprising at least one labeling moiety.
 152. The conjugate of claim 151 wherein the labeling moiety is selected from the group consisting of fluorescent moieties, quencher moieties, visible dye moieties, radioactive moieties, chemiluminescent moieties, biotin moieties, hapten moieties, micro-particles, paramagnetic micro-particles, and enzymatic labeling moieties.

153. The conjugate of claim 152 wherein the labeling moiety is a fluorescent dye moiety selected from the group consisting of: BODIPY™ dyes, cyanine dyes, Alexa™ dyes, fluorescein dyes, rhodamine dyes, phycoerythrin dyes, coumarin dyes, Texas Red dyes, Lissamine™, FAM, HEX, TET, TAMRA, ROX, EDANA, 4-Acetamido-4'-isothiocyanato-stilbene-2,2'-disulfonic acid, 4,4'-Diisothiocyanatostilbene-2,2'-disulfonic acid, Succinimidyl pyrene butyrate, Acridine isothiocyanate, Cascade Blue, Oregon Green, Lucifer Yellow vinyl sulfone, and IR1446 (Kodak™ Laser Dye).
- 5
154. The conjugate of claim 152 wherein the labeling moiety is a quencher moiety selected from the group consisting of Black Hole Quencher™ moieties, DABCYL, Reactive Red 4 (Cibacron Brilliant Red 3B-A), Malachite Green, 4-Dimethylaminophenylazophenyl-4'-isothiocyanate (DABITC), and 4,4'-Diisothiocyanatodihydro-stilbene-2,2'-disulfonic acid moieties.
- 10
155. A supermolecular construct comprising at least one conjugate of claim 102 and at least one synthetic address unit (SAU) which is specifically associated with at least one SBU of the conjugate to form a synthetic binding system unit (SBS), wherein the SAU is attached to a support material (SM.)
- 15
156. The supermolecular construct of claim 155 wherein the SBU and the SAU each comprise an at least partially complementary sequence of monomeric units which non-covalently associate with one another in a sequence-dependent manner.
- 20
157. The supermolecular construct of claim 155, wherein the synthetic address unit (SAU) comprises, independently of the synthetic binding unit (SBU), an oligomer selected from the group consisting of p-RNAs, p-DNAs and CNAs.
158. The supermolecular construct of claim 155 wherein the support is a bead.
- 25
159. The supermolecular construct of claim 155, comprising at least two conjugates, wherein each conjugate is specifically associated with at least one synthetic address unit (SAU) by a molecular interaction with the SBU of each conjugate, to form at least two synthetic binding system units (SBS), wherein each SAU is attached to a support material (SM) at a predetermined location.
- 30
160. The supermolecular construct of claim 159 comprising at least five conjugates.
161. The supermolecular construct of claim 159 comprising at least ten conjugates.

- 162. The supermolecular construct of claim 159 comprising at least 100 conjugates.
- 163. The supermolecular construct of claim 159 comprising at least 1000 conjugates.
- 164. The supermolecular construct of claim 159 wherein the support is a planar surface.
- 5 165. The supermolecular construct of claim 164 wherein the planar surface comprises an array of discrete locations, wherein each SAU is attached to a predetermined location in the array.
- 166. The supermolecular construct of claim 165 wherein each discreet location has a single SAU attached at that location.
- 10 167. The supermolecular construct of claim 165 wherein at least one discreet location has a known mixture of SAUs attached at that location.
- 168. The supermolecular construct of claim 165 wherein a plurality of discreet locations have the same SAU or mixture of SAUs attached at the locations.
- 169. The supermolecular construct of claim 159 wherein the support material is the surface of a sensor for surface plasmon resonance measurements.
- 15 170. The supermolecular construct of claim 159 wherein the support material comprises a material selected from the group consisting of silicon, silicon dioxide, silicon nitride, controlled porosity glass, metal, metal silicilide, inorganic sol-gels, and hydrogels.
- 20 171. The supermolecular construct of claim 159 wherein the support material comprises a hydrogel selected from the group consisting of agarose, polyacrylamide, polymethacrylamide, and organic polymer hydrogels.
- 172. The supermolecular construct of claim 159 wherein the support material is a permeation layer over an electrode of an active electronic array.
- 25 173. The supermolecular construct of claim 159 wherein the synthetic address units (SAU) are attached to the support material via a biotin/streptavidin interaction.
- 174. The supermolecular construct of claim 159 wherein the synthetic address units (SAU) are attached to the support material via at least one covalent bond.

175. The supermolecular construct of claim 174 wherein the covalent bond is formed by reacting a hydrazide group on the synthetic address units (SAU) with a functional group on the support.
176. A library comprising at least two conjugates of claim 102.
- 5 177. The library of claim 176, wherein the SBU portions of the conjugate members of the library are orthogonal.
178. The library of claim 176, wherein the library comprises at least five conjugates.
179. The library of claim 178, wherein the SBU portions of the conjugate members of the library are orthogonal
- 10 180. The library of claim 176, wherein the library comprises at least ten conjugates.
181. The library of claim 180, wherein the SBU portions of the conjugate members of the library are orthogonal
182. The library of claim 176, wherein the library comprises at least twenty conjugates.
183. The library of claim 176, wherein the library comprises at least 100 conjugates.
- 15 184. The library of claim 176, wherein each NA sequence in the library is conjugated to a specific SBU.
185. The library of claim 176, wherein each SBU in the library is conjugated to a specific NA sequence.
- 20 186. The library of claim 176, wherein each NA sequence in the library is conjugated to a specific SBU, and each SBU is conjugated to a specific NA sequence.
187. The library of claim 176, wherein each NA sequence in the library is conjugated to a set of SBUs.
188. The library of claim 176, wherein each SBU is conjugated to a set of NA sequences.
- 25 189. The conjugate of claim 102, wherein at least one (SBU) comprises an oligomer of monomeric units, wherein the monomeric units have the general formula



wherein B_b is a backbone moiety which connects the monomeric unit to the oligomer, and wherein R^s is a specific recognition moiety comprising a nitrogen heterocycle moiety,

5 wherein the monomeric units linearly arranged according to the formulae (IX) or (X),

$B_{s1}-(J)-B_{s2}$ (formula (IX))
 $B_{s1}-(J)-B_{s2}-(J')-B_{s3}$ (formula (X))

10 wherein s_1 , s_2 and s_3 are, independently, an integer between 0 and 10, and B is any monomeric unit as is used for synthesizing the synthetic binding units (SBU), and J is a sequence of recognition moieties (R^s), wherein J may be the same or different than J' , and

15 wherein the sequences J and J' are, independently, selected from group A consisting of SEQ. ID Nos. 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, and 75, or are selected from the group B consisting of SEQ. ID Nos. 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, and 76, provided that sequences J and J' are selected from the same group.

- 20
- 25
190. A method of producing a set of immobilized nucleic acids on a support material comprising:
a) providing a support material, wherein synthetic address units (SAU) are attached at predetermined positions on the support,
b) contacting at least two conjugates of claim 102, wherein the conjugates comprise at least one SBU which specifically binds to at least one SAU on the support, with the support under conditions suitable for the association of SBU's and SAU's to form SBS's.

- 5
- 191. The method of claim 190 wherein a plurality of conjugates are contacted with the support material at the same time.
 - 192. The method of claim 191 wherein at least some of the conjugates are contacted with the support sequentially in a number of M incubation steps, wherein the support is washed to remove non-immobilized conjugates between each of M steps.
 - 193. The method of claim 192 M is an integer between 2 and 100.
 - 194. The method of claim 192 M is an integer between 2 and 20.
 - 195. The method of claim 192 M is an integer between 2 and 10.

10

 - 196. The method of claim 190 wherein the synthetic address unit (SAU) is attached to the support material via a biotin/streptavidin interaction.
 - 197. The method of claim 190 wherein the synthetic address units (SAU) are attached to the support material via at least one covalent bond.
 - 198. The method of claim 197 wherein the covalent bond is formed by reacting a hydrazide group on the synthetic address units (SAU) with a functional group on the support.

15

 - 199. The method of claim 190 wherein the support material is a silicon-containing substrate.
 - 200. The method of claim 190 wherein the support material is the surface of a sensor for surface plasmon resonance measurements.

20

 - 201. The method of claim 190 wherein the support material comprises a material selected from the group consisting of silicon, silicon dioxide, silicon nitride, controlled porosity glass, metal, metal silicilide, inorganic sol-gels, and hydrogels.
 - 202. The method of claim 190 wherein the support material comprises a hydrogel selected from the group consisting of agarose, polyacrylamide, polymethacrylamide, and organic polymer hydrogels.

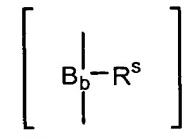
25

 - 203. The method of claim 190 wherein the support material is a permeation layer over an electrode of an active electronic array.
 - 204. The method of claim 203 wherein at least some of the electrodes in the active electronic array are electrically biased during step (b).

30

205. The method of claim 190, wherein the conjugates are contacted with a sample before being contacted with the support.
206. The method of claim 205 wherein the sample is a biological sample.
207. The method of claim 206 wherein the biological sample is derived from a sample selected from the group consisting of human materials, animal materials, plant materials, fungal materials, cell cultures, viral cultures, food samples, and water samples.
208. The method of claim 206 wherein more than one set of conjugates is contacted with more than one biological sample, wherein nucleic acids of each biological sample which hybridize to nucleic acids of the conjugates are sorted by the SBUs of the conjugates to known locations on the support material.
209. The method of claim 208 wherein the same nucleic acids of the conjugates are conjugated to a corresponding different SBU in each set of SBUs.
210. The method of claim 208 wherein each biological sample is obtained under differing conditions for the biological material sampled, and wherein the sorting of the hybridized nucleic acids from each sample by the pairing of the SBUs to the SAUs produces a gene expression pattern.
211. The method of claim 190, further comprising incubating the support with a sample containing targets and with reagents for detecting binding of targets to the conjugates.
212. The method of claim 211 wherein the sample is a biological sample.
213. The method of claim 212 wherein the biological sample is derived from a sample selected from the group consisting of human materials, animal materials, plant materials, fungal materials, cell cultures, viral cultures, food samples, and water samples.
214. The method of claim 211 further comprising the step of detecting the target nucleic acids hybridized to the nucleic acids of conjugates immobilized on the support material.
215. The method of claim 214 further comprising the step of removing, after detecting the hybridized nucleic acids, the conjugates and sample from the support material by destabilizing the association between the SBUs and the SAUs.

216. The method of claim 215 wherein the conjugates are removed by contacting the array with a denaturing agent solution.
217. The method of claim 215 wherein the conjugates are removed by contacting the array with a basic solution
- 5 218. The method of claim 217 wherein the basic solution is selected from the group consisting of a sodium hydroxide solution, a potassium hydroxide solution, and an ammonia solution.
219. The method of claim 218 wherein the concentration of sodium hydroxide in solution is from about 1.0 mM to about 100 mM.
- 10 220. The method of claim 218 wherein the concentration of sodium hydroxide in solution is about 10 mM.
221. A unit of a synthetic binding system selected from the group consisting of a synthetic binding unit (SBU) and a synthetic addressing unit (SAU), comprising an oligomer of monomeric units, wherein the monomeric units have the general



15 formula

wherein B_b is a backbone moiety which connects the monomeric unit to the oligomer, and wherein R^s is a specific recognition moiety comprising a nitrogen heterocycle moiety,

20 wherein the monomeric units linearly arranged according to the formulae (IX) or (X),

$B_{s1}-(J)-B_{s2}$ (formula (IX))

$B_{s1}-(J)-B_{s2}-(J')-B_{s3}$ (formula (X))

25 wherein $s1$, $s2$ and $s3$ are, independently, an integer between 0 and 10, and B is any monomeric unit as is used for synthesizing the synthetic binding units (SBU),

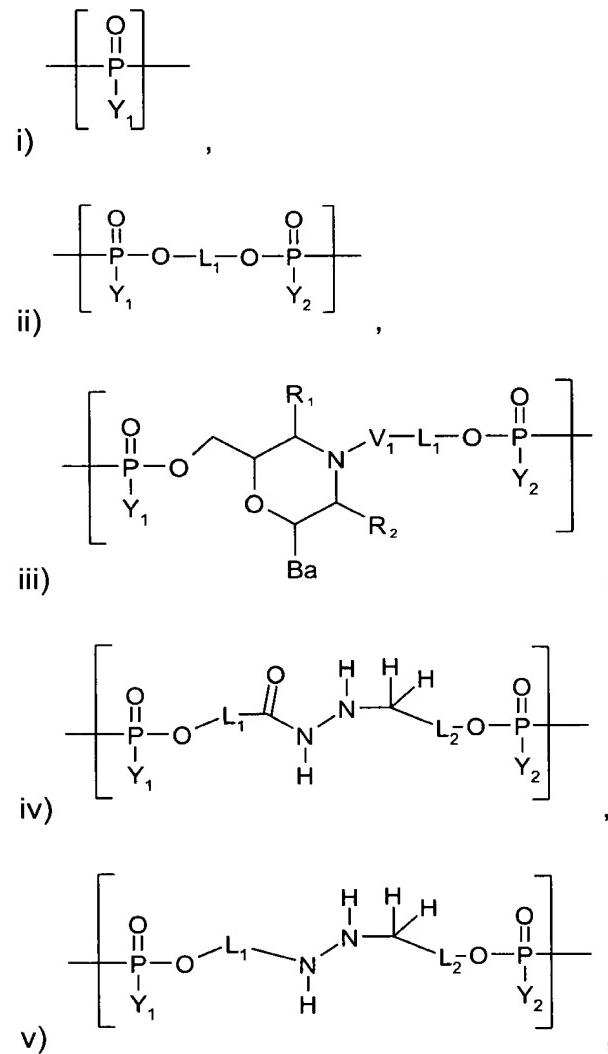
and J is a sequence of recognition moieties (R^s), wherein J may be the same or different than J', and

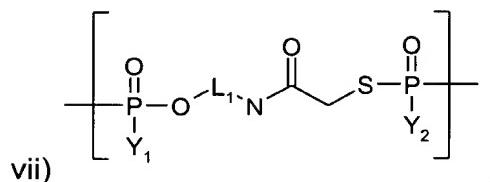
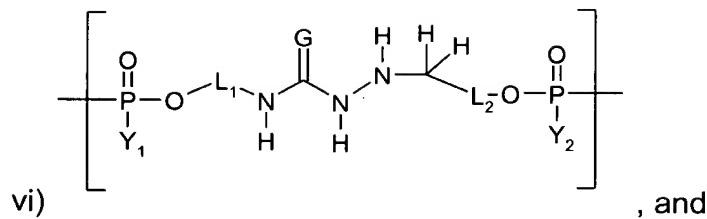
wherein the sequences J and J' are, independently, selected from group A consisting of SEQ. ID Nos. 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, and 75, or are selected from the group B consisting of SEQ. ID Nos. 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, and 76, provided that sequences J and J' are selected from the same group.

- 10 222. The unit of claim 221 wherein J and J' are, independently, selected from group A' consisting of SEQ. ID Nos. 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, and 47, or are selected from the group B' consisting of sequences SEQ. ID Nos. 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, and 48, provided that sequences J and J' are selected from the same group.
- 15 223. The unit of claim 221 wherein J and J' are, independently, selected from group A" consisting of SEQ. ID Nos. 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, and 75, or are selected from the group B" consisting of sequences SEQ. ID Nos. 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, and 76, provided that sequences J and J' are selected from the same group.
- 20 224. The unit of claim 221 wherein J and J' are, independently, selected from group A''' consisting of SEQ. ID Nos. 49, 51, 53, 57, 59, 61, 65, 69, 71, and 75, or are selected from the group B''' consisting of sequences SEQ. ID Nos. 50, 52, 54, 58, 60, 62, 66, 70, 72, and 76, provided that sequences J and J' are selected from the same group.
- 25 225. A kit for immobilizing biomolecules comprising the at least two synthetic binding units (SBUs) of claim 221 wherein the synthetic binding units are orthogonal.
226. The kit of claim 225 comprising at least five SBUs.
227. The kit of claim 225 comprising at least ten SBUs.
- 30 228. The kit of claim 225 comprising at least twenty SBUs.

229. The kit of any one of claims 225 to 228 wherein the SBUs comprise a functional group for conjugation with a biomolecule.
230. The kit of claim 229 wherein the functional group is selected from the group consisting of amines, hydrazides, aldehydes, hydrazines, and semicarbazides.
- 5 231. The kit of claim 229 wherein the functional group is a hydrazide.
232. The kit of claim 229 wherein each SBU is conjugated to a nucleic acid (NA).
233. The kit of claim 232 wherein the conjugation is through a linker moiety X or a branching moiety W, wherein

X, independently for each linker unit, is selected from the group consisting of:





wherein

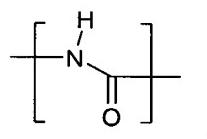
Y_1, Y_2 are independently of one another OH; SH, NH₂ or CH₃,

G is O or S,

L_1, L_2 are independently linkers selected from the group consisting of:
a covalent bond; and a linker chain moiety comprising a saturated or unsaturated, branched or unbranched, substituted or unsubstituted, chain of 1-60 carbon atoms and 0-40 heteroatoms selected from the group consisting of N, O, and S;

V_1, V_2 are independently selected from the group consisting of

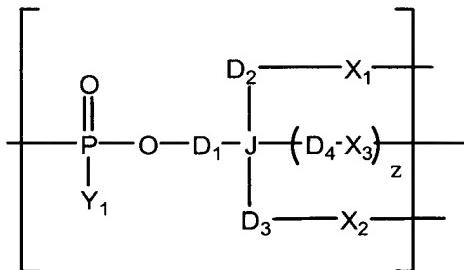
-[CH₂]-, and



R_1, R_2 are independently of one another H or OH, and

Ba is a nitrogen heterocycle moiety;

and wherein W has the general formula:



wherein Y₁ is OH, SH, NH₂ or CH₃;

wherein D₁, D₂, D₃, and D₄, are, independently, a covalent bond or a linker chain moiety comprising a saturated or unsaturated, branched or unbranched, substituted or unsubstituted, chain of 1 to 10 carbon atoms and 0 to 4 heteroatoms selected from the group consisting of O, S, and N;

wherein J is carbon or nitrogen;

wherein z is 0 or 1, further wherein z is 0 if J is nitrogen; and

wherein X₁, X₂, and X₃, are independently X as described above.

234. The kit of claim 232 wherein each nucleic acid in the kit is conjugated to a different SBU.
- 5 235. The kit of claim 232 wherein each nucleic acid in the kit is conjugated to a different set of SBUs.
236. The kit of claim 232 wherein each SBU in the kit is conjugated to a different set of nucleic acids.
- 10 237. The kit of claim 232 wherein each SBU in the kit is conjugated to a different nucleic acid.
238. The kit of claim 232 wherein the synthetic binding units (SBU) are, independently, selected from the group consisting of p-RNAs, p-DNAs, and CNA's.

239. The kit of claim 232 wherein the nucleic acid (NA) is selected from the group consisting of deoxyribonucleic acids and ribonucleic acids, and chemically modified nucleic acids.
240. The kit of claim 232 wherein the nucleic acid (NA) is selected from the group consisting of peptide nucleic acids (PNA) and locked nucleic acids (LNA.)
- 5 241. The kit of claim 232 wherein the conjugates further comprising at least one labeling moiety.
- 10 242. The kit of claim 241 wherein the labeling moiety is selected from the group consisting of fluorescent moieties, quencher moieties, visible dye moieties, radioactive moieties, chemiluminescent moieties, biotin moieties, hapten moieties, micro-particles, paramagnetic micro-particles, and enzymatic labeling moieties.
- 15 243. A kit for immobilizing biomolecules comprising at least two synthetic addressing units (SAUs) of claim 221 wherein the synthetic addressing units are orthogonal.
244. The kit of claim 243 comprising at least five SAUs.
245. The kit of claim 243 comprising at least ten SAUs.
246. The kit of claim 243 comprising at least twenty SAUs.
247. The kit of claim 243 wherein the SAUs comprise a functional group for attachment to a support material.
- 20 248. The kit of claim 247 wherein the functional group is selected from the group consisting of amines, hydrazides, aldehydes, hydrazines, carbamides, and carbamines.
249. The kit of claim 247 wherein the functional group is a hydrazide.
250. The kit of claim 247 wherein the functional group is biotin.
- 25 251. The kit of claim 243 wherein each SAU is attached on a support material at a known location.
252. The kit of claim 251 wherein each SAU is attached at a different location.
253. The kit of claim 251 wherein each SAU is attached at a known set of locations.

254. The kit of claim 251 wherein between 1 and 100 different SAUs are attached at known locations.
255. The kit of claim 251 wherein between 2 and 20 different SAUs are attached at known locations.
- 5 256. The kit of claim 251 wherein between 2 and 10 different SAUs are attached at known locations.
257. The kit of claim 251 wherein the support comprises a silicon-based substrate.
258. The kit of claim 251 wherein the support material is the surface of a sensor for surface plasmon resonance measurements.
- 10 259. The kit of claim 251 wherein the support material comprises a material selected from the group consisting of silicon, silicon dioxide, silicon nitride, controlled porosity glass, metal, metal silicilide, inorganic sol-gels, and hydrogels.
260. The kit of claim 251 wherein the support material comprises a hydrogel selected from the group consisting of agarose, polyacrylamide, polymethacrylamide, and organic polymer hydrogels.
- 15 261. The kit of claim 251 wherein the support material is a permeation layer over an electrode of an active electronic array.
262. The kit of claim 251 wherein the synthetic address units (SAU) are attached to the support material via a biotin/streptavidin interaction.
- 20 263. The kit of claim 251 wherein the synthetic address units (SAU) are attached to the support material via at least one covalent bond.
264. The kit of claim 263 wherein the covalent bond is formed by reacting a hydrazide group on the synthetic address units (SAU) with a functional group on the support.
- 25 265. An improved method for preparing conjugates of nucleic acids with synthetic binding units, the method comprising:
a) synthesizing the conjugates on a solid support phase using monomer or oligomer units, wherein the units are β -cyanoethyl-protected on at least one phosphorus of the units,

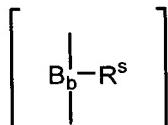
- b) treating the support with a solution of an alkylamine in an inert solvent,
- c) treating the support with hydrazine to cleave off and deprotect the conjugate.
- 5 266. The method of claim 265 wherein the alkylamine is a secondary alkylamine.
267. The method of claim 265 wherein the alkylamine is selected from the group consisting of dimethylamine, diethylamine, dipropylamine, dibutylamine, dipentylamine, dihexylamine, di-N-octylamine, di-N-decylamine, didodecylamine, N-ethylmethylamine, N-methyl-N-propylamine, N-methylbutylamine, N-methylpentylamine, N-methylhexylamine, N-ethylpropylamine, N-(N-butyl)-N-propylamine, N-amyl-N-butylamine, N,N'-di-N-butyl-1,6-hexanediamine, N,N'-dimethyl-1,3-propanediamine, N,N'-dimethyl-1,6-hexanediamine.
- 10 268. The method of claim 265 wherein the alkylamine is diethylamine.
269. The method of claim 265 wherein the alkylamine is present in solution at about 0.2% to about 10%.
- 15 270. The method of claim 265 wherein the alkylamine is present in solution at about 1% to about 5%.
271. The method of claim 265 wherein the alkylamine is present in solution at about 1.5%.
- 20 272. The method of claim 265 wherein the inert solvent is selected from the group consisting of dichloromethane, chloroform, carbon tetrachloride, dichlorethane, tetrahydrofuran, toluol, diethylether, ethanol, methanol, acetonitrile, hexane, and heptane.
273. The method of claim 265 wherein the inert solvent is dichloromethane.
- 25 274. The method of claim 265 wherein the alkylamine is 1.5% diethylamine in dichloromethane. .
275. A method for enzymatically modifying a nucleic acid selected from the group consisting of a target nucleic acid and the nucleic acid of a conjugate comprising at least one nucleic acid (NA) and at least one synthetic binding unit (SBU), utilizing the nucleic acid of the conjugate as a substrate, the method comprising:

- a) contacting the conjugate with at least one enzyme which utilizes naturally occurring nucleic acids as a substrate, and with other reagents necessary for the action of the enzyme; and
- b) incubating the mixture obtained in a) under conditions suitable for the functioning of the enzyme for a period of time sufficient to effect the modification of the nucleic acid.
- 5 276. The method of claim 275 wherein the other reagents include a nucleic acid which hybridizes to the NA of the conjugate.
- 10 277. The method of claim 275 wherein the other reagents include nucleoside triphosphates or modified nucleoside triphosphates.
278. The method of claim 275 wherein at least one enzyme is selected from the group consisting of a polymerase, a ligase, an endonuclease, an exonuclease, a kinase, a methyltransferase, a methylase, a restriction endonuclease, and a terminal transferase.
- 15 279. The method of claim 275 wherein the enzyme is a ligase, and the NA of the conjugate is modified by ligation of a terminus of the NA to at least one additional nucleic acid.
- 20 280. The method of claim 279 wherein the ligation is template-dependent, and wherein the NA of the conjugate and the additional nucleic acid are hybridized to adjacent sequences of a template nucleic acid.
281. The method of claim 279 wherein the ligation is template-independent, and wherein the NA of the conjugate and the additional nucleic acid are single stranded.
282. The method of claim 281 wherein the ligase used is a T4 RNA ligase.
- 25 283. The method of claim 279 wherein the ligation is a blunt-end, and wherein the NA of the conjugate and the additional nucleic acid are double stranded.
284. The method of claim 275 wherein the enzyme is a polymerase, wherein the NA of the conjugate has an unblocked 3' terminus, wherein the other reagents comprise a template nucleic acid to which the unblocked 3' terminus of the NA hybridizes, and wherein the NA is modified by the addition of at least one nucleoside complementary to the template nucleic acid to the 3' terminus of the NA.

285. The method of claim 284 wherein a dideoxynucleotide is added to the NA of the conjugate.
286. The method of claim 284 wherein a labeled nucleotide is added to the NA of the conjugate.
- 5 287. The method of claim 284 wherein the template nucleic acid is derived from a biological sample.
- 10 288. The method of claim 287 wherein the biological sample is derived from a sample selected from the group consisting of human materials, animal materials, plant materials, fungal materials, cell cultures, viral cultures, food samples, and water samples.
- 15 289. The method of claim 284 wherein the polymerase is at least one enzyme selected from the group consisting of DNA polymerases, RNA polymerases, and reverse transcriptases.
- 20 290. The method of claim 284 wherein at least a portion of the template nucleic acid sequence is amplified.
- 25 291. The method of claim 284 wherein the polymerase is a thermostable polymerase, and wherein the conditions of b) comprise thermocycling the mixture of a) to alternately i) dissociate extension products from the template nucleic acid and ii) allow the hybridization of conjugate NA to the template and enzymatic extension of the NA of the conjugate, wherein at least a portion of the template nucleic acid sequence is amplified.
- 30 292. The method of claim 284, further comprising contacting the conjugate with a restriction endonuclease in the mixture of a), wherein the NA of the conjugate comprises an endonuclease recognition sequence 5' of the 3' terminus which hybridizes to the template nucleic acid, and wherein at least a portion of the template nucleic acid sequence is amplified by strand displacement amplification.
293. The method of claim 284, wherein the polymerase is a mixture of an RNA polymerase and a reverse transcriptase, further comprising contacting the conjugate with an RNase H activity in the mixture of a), wherein at least a portion of the template nucleic acid sequence is amplified by transcription mediated amplification.

294. The method of claim 275 wherein the enzyme is a terminal transferase, and the NA of the conjugate is modified by addition of at least one nucleoside to the 3' terminus of the NA.
295. The method of claim 294 wherein a labeled nucleoside is added to the NA of the conjugate.
296. The method of claim 294 wherein a homopolymeric tail is added to the NA of the conjugate.
297. The method of claim 275 wherein the enzyme is a restriction endonuclease, wherein the other reagents comprise a target nucleic acid to which at least a portion of the NA of the conjugate hybridizes, and wherein the NA of the conjugate and the target nucleic acid are cleaved by the restriction endonuclease in step (b).
298. The method of claim 275 wherein the enzyme is a restriction endonuclease, wherein the other reagents comprise a target nucleic acid to which at least a portion of the NA of the conjugate hybridizes, and wherein the NA of the conjugate but not the target nucleic acid is cleaved by the restriction endonuclease in step (b).
299. The method of claim 275 wherein the enzyme is a restriction endonuclease, wherein the other reagents comprise a target nucleic acid to which at least a portion of the NA of the conjugate hybridizes, and wherein the target nucleic acid but not the NA of the conjugate is cleaved by the restriction endonuclease in step (b).
300. The method of claim 275 wherein the enzyme is a RNase H, wherein the other reagents comprise an RNA target nucleic acid to which at least a portion of the NA of the conjugate hybridizes, and wherein the target RNA nucleic acid hybridizing to the NA of the conjugate is degraded by the RNase H in step (b).
301. The method of claim 275 wherein the point of activity of the enzyme is within 30 nucleotides of the point of conjugation of the NA with the SBU.
302. The method of claim 275 wherein the point of activity of the enzyme is within 20 nucleotides of the point of conjugation of the NA with the SBU.

303. The method of claim 275 wherein the point of activity of the enzyme is within 15 nucleotides of the point of conjugation of the NA with the SBU.
304. The method of claim 275 wherein the point of activity of the enzyme is within 10 nucleotides of the point of conjugation of the NA with the SBU.
- 5 305. The method of claim 275 wherein the point of activity of the enzyme is within 7 nucleotides of the point of conjugation of the NA with the SBU.
306. The method of claim 275 wherein the point of activity of the enzyme is within 5 nucleotides of the point of conjugation of the NA with the SBU.
- 10 307. The method of claim 275 wherein the point of activity of the enzyme is within 2 nucleotides of the point of conjugation of the NA with the SBU.
308. The method of claim 275 wherein the point of activity of the enzyme is the nucleotide at the point of conjugation of the NA with the SBU.
309. The method of claim 275 wherein at the SBU is an oligomer comprised of monomeric units, the monomeric units having the general formula:



15 wherein B_b is a backbone moiety which connects the monomeric unit to the oligomer, and wherein R^s is a specific recognition moiety which provides the molecular interaction which allows the SBU to specifically interact with a synthetic addressing unit.

- 20 310. The method of claim 309 wherein B_b comprises a 6 membered ring containing carbon.
311. The method of claim 309 wherein B_b comprises a six membered ring selected from the group consisting of a pyranosyl ring and a cyclohexyl ring.
- 25 312. The method of claim 309 wherein R^s provides the molecular interaction through hydrogen bonds or base stacking.
313. The method of claim 309 wherein R^s comprises a nitrogen heterocycle moiety.

314. The method of claim 309 wherein at least one synthetic binding unit (SBU) is selected from the group consisting of p-RNAs, p-DNAs, and CNA's.
315. The method of claim 314 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 2' end with the 5' end of the nucleic acid (NA).
- 5 316. The method of claim 314 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 2' end with the 3' end of the nucleic acid (NA).
- 10 317. The method of claim 314 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 4' end with the 3' end of the nucleic acid (NA).
318. The method of claim 314 wherein the synthetic binding unit (SBU) is pRNA or pDNA, and wherein the SBU is linked via its 4' end with the 5' end of the nucleic acid (NA).
- 15 319. The method of claim 275 wherein the nucleic acid (NA) is selected from the group consisting of deoxyribonucleic acids, ribonucleic acids, and chemically modified nucleic acids.
320. The method of claim 275 wherein the nucleic acid (NA) is selected from the group consisting of phosphorothioate nucleic acids, phosphorodithioate nucleic acids, methylphosphonate nucleic acids, 2'-O-methyl RNA, and 2'-fluoro RNA.
- 20 321. The method of claim 275 wherein the nucleic acid (NA) is selected from the group consisting of peptide nucleic acids (PNA) and locked nucleic acids (LNA.)
322. The method of claim 275 wherein the nucleic acid (NA) is selected from the group consisting of an aptamer and an aptazyme.
- 25 323. The method of claim 275 wherein the conjugate further comprises at least one labeling moiety.
324. The method of claim 323 wherein the labeling moiety is selected from the group consisting of fluorescent moieties, quencher moieties, visible dye moieties, radioactive moieties, chemiluminescent moieties, biotin moieties, hapten moieties, micro-particles, paramagnetic micro-particles, and enzymatic labeling moieties.
- 30

325. The method of claim 323 wherein the labeling moiety is a fluorescent dye moiety selected from the group consisting of: BODIPY™ dyes, cyanine dyes, Alexa™ dyes, fluorescein dyes, rhodamine dyes, phycoerythrin dyes, coumarin dyes, Texas Red dyes, Lissamine™, FAM, HEX, TET, TAMRA, ROX, EDANA, 4-Acetamido-4'-isothiocyanato-stilbene-2,2'-disulfonic acid, 4,4'-Diisothiocyanatostilbene-2,2'-disulfonic acid, Succinimidyl pyrene butyrate, Acridine isothiocyanate, Cascade Blue, Oregon Green, Lucifer Yellow vinyl sulfone, and IR1446 (Kodak™ Laser Dye).
 326. The method of claim 323 wherein the labeling moiety is a quencher moiety selected from the group consisting of Black Hole Quencher™ moieties, DABCYL, Reactive Red 4 (Cibacron Brilliant Red 3B-A), Malachite Green, 4-Dimethylaminophenylazophenyl-4'-isothiocyanate (DABITC), and 4,4'-Diisothiocyanatodihydro-stilbene-2,2'-disulfonic acid moieties.